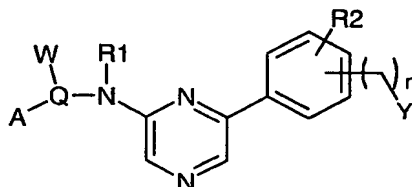


71.

CLAIMS

1. A method of modulating microtubule polymerisation in a subject, said method comprising administering a therapeutically effective amount of at least one compound of the general formula (I)



I

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

R^1 is H, C_{1-4} alkyl;

Q is a bond, or C_{1-4} alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C_{1-4} alkyl, CH_2F , CHF_2 , CF_3 , CN, aryl, hetaryl, OCF_3 , $OC_{1-4}alkyl$, $OC_{2-5}alkylINR^4R^5$, $Oaryl$, $Ohetaryl$, CO_2R^4 , $CONR^4R^5$, nitro, NR^4R^5 , $C_{1-4}alkylINR^4R^5$, $NR^6C_{1-4}alkylINR^4R^5$, NR^4COR^5 , $NR^6CONR^4R^5$, $NR^4SO_2R^5$;

R^4 , R^5 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, $C_{1-4}alkyl$ aryl, $C_{1-4}alkyl$ hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR⁷;

R^6 is selected from H, C_{1-4} alkyl;

R^7 is selected from H, C_{1-4} alkyl, aryl, hetaryl, $C_{1-4}alkyl$ aryl, $C_{1-4}alkyl$ hetaryl;

R^2 is 0-2 substituents independently selected from halogen, $C_{1-4}alkyl$, OH, $OC_{1-4}alkyl$, CH_2F , CHF_2 , CF_3 , OCF_3 , CN, $C_{1-4}alkylINR^8R^9$, $OC_{1-4}alkylINR^8R^9$, CO_2R^8 , $CONR^8R^9$, NR^8R^9 , NR^8COR^9 , $NR^{10}CONR^8R^9$, $NR^8SO_2R^9$;

72.

R8, R9 are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, aryl, hetaryl, C₁₋₄ alkyl aryl, C₁₋₄ alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR11;

R10 is selected from H, C₁₋₄ alkyl, aryl or hetaryl;

R11 is selected from H, C₁₋₄ alkyl, aryl, hetaryl, C₁₋₄ alkyl aryl, C₁₋₄ alkyl hetaryl;

Y is halogen, OH, NR12R13, NR14COR12, NR14CONR12R13, N14SO₂R13;

R12 and R13 are each independently H, CH₂F, CHF₂, CF₃, CN, C₁₋₄ alkyl optionally substituted with OH, OC₁₋₄alkyl or NR15R16, cycloalkyl; cyclohetalkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, or may be joined to form an optionally substituted 3-6 membered ring optionally containing an atom selected from O, S, NR14

R14, R15 and R16 are each independently selected from H, C₁₋₄ alkyl;

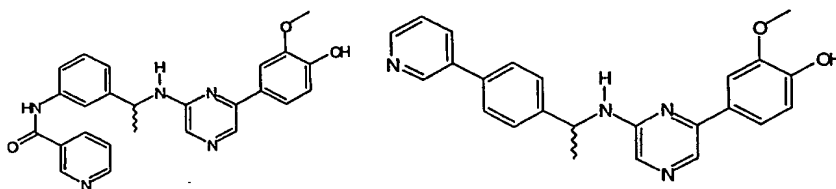
n = 0-4;

W is selected from H, C₁₋₄alkyl, C₂₋₆alkenyl; where C₁₋₄alkyl or C₂₋₆alkenyl may be optionally substituted with C₁₋₄alkyl, OH, OC₁₋₄alkyl, NR15R16;

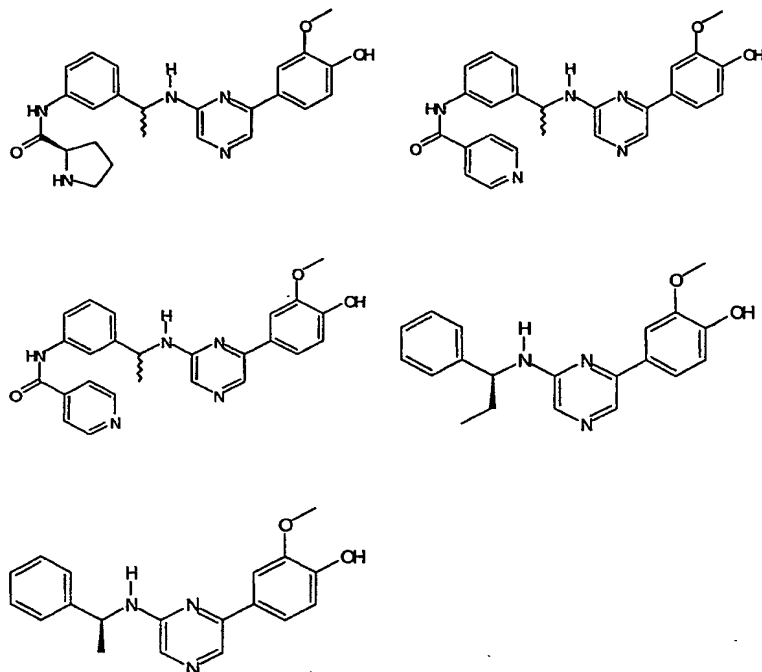
R15, and R16 are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17;

R17 is selected from H, C₁₋₄ alkyl.

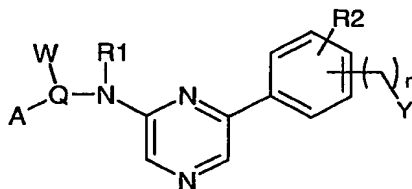
2. A method according to claim 1 wherein the compound is selected from the group consisting of:



73.



3. A method according to claim 1 or claim 2, wherein said method is used in the treatment of a hyperproliferation-related disorder or disease state.
4. A method according to claim 2, wherein the hyperproliferation-related disorder or disease state is selected from the group consisting of Cancer, infectious diseases, vascular restenosis and inflammatory diseases.
5. A compound of the general formula (II)



II

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

74.

R1 is H, C₁₋₄ alkyl;Q is a bond, or C₁₋₄ alkyl;

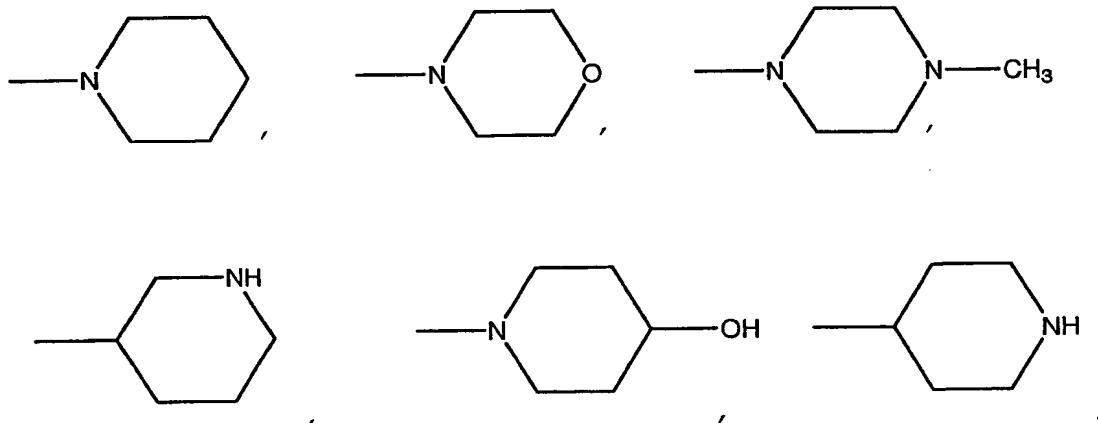
A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CH₂F, CHF₂, CF₃, CN, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR₄R₅, Oaryl, Ohetaryl, CO₂R₄, CONR₄R₅, nitro, NR₄R₅, C₁₋₄ alkylNR₄R₅, NR₆C₁₋₄alkylNR₄R₅, NR₄COR₅, NR₆CONR₄R₅, NR₄SO₂R₅;

R₄, R₅ are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, aryl, hetaryl, C₁₋₄alkyl aryl, C₁₋₄ alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₇;

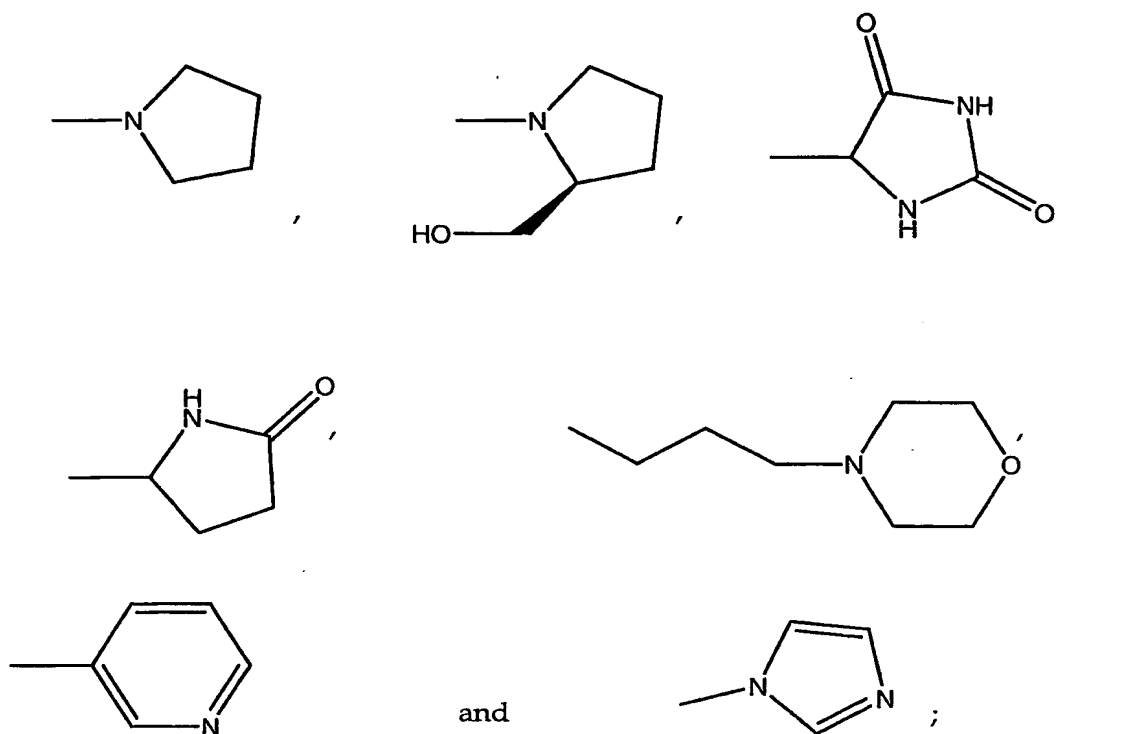
R₆ is selected from H, C₁₋₄ alkyl;R₇ is selected from H, C₁₋₄ alkyl, aryl, hetaryl, C₁₋₄ alkyl aryl, C₁₋₄ alkyl hetaryl;R₂ is 0-2 substituents independently selected from C₁₋₄alkyl and OC₁₋₄alkyl;

Y is CH₂OH, OC₁₋₄alkylOH, OC₁₋₄alkylR₁₂, OC₁₋₄alkylNR₁₂NR₁₃, C(O)R₁₂, CH₂R₁₂, COOR₁₂, CONR₁₂R₁₃, OCONR₁₂R₁₃, CH₂NR₁₂R₁₃, NHCOR₁₂, NHCONR₁₂R₁₃,

R₁₂ and R₁₃ are each independently H, C₁₋₂ alkyl, (CH₂)₃NEt₂, (CH₂)₂NMe₂, (CH₂)₅NH₂, (CH₂)₂OH,



75.



n = 0-4;

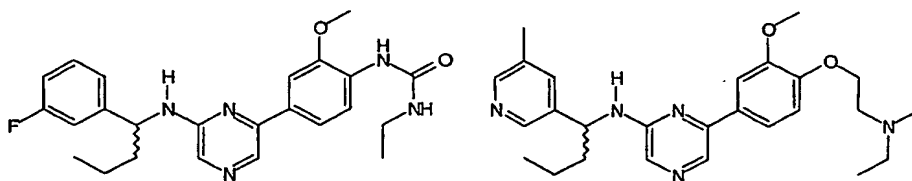
W is selected from H, C₁₋₄alkyl, C₂₋₆alkenyl; where C₁₋₄alkyl or C₂₋₆alkenyl may be optionally substituted with C₁₋₄alkyl, OH, OC₁₋₄alkyl, NR₁₅R₁₆;

R₁₅, and R₁₆ are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cycloalkyl, C₁₋₄ alkyl cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₁₇

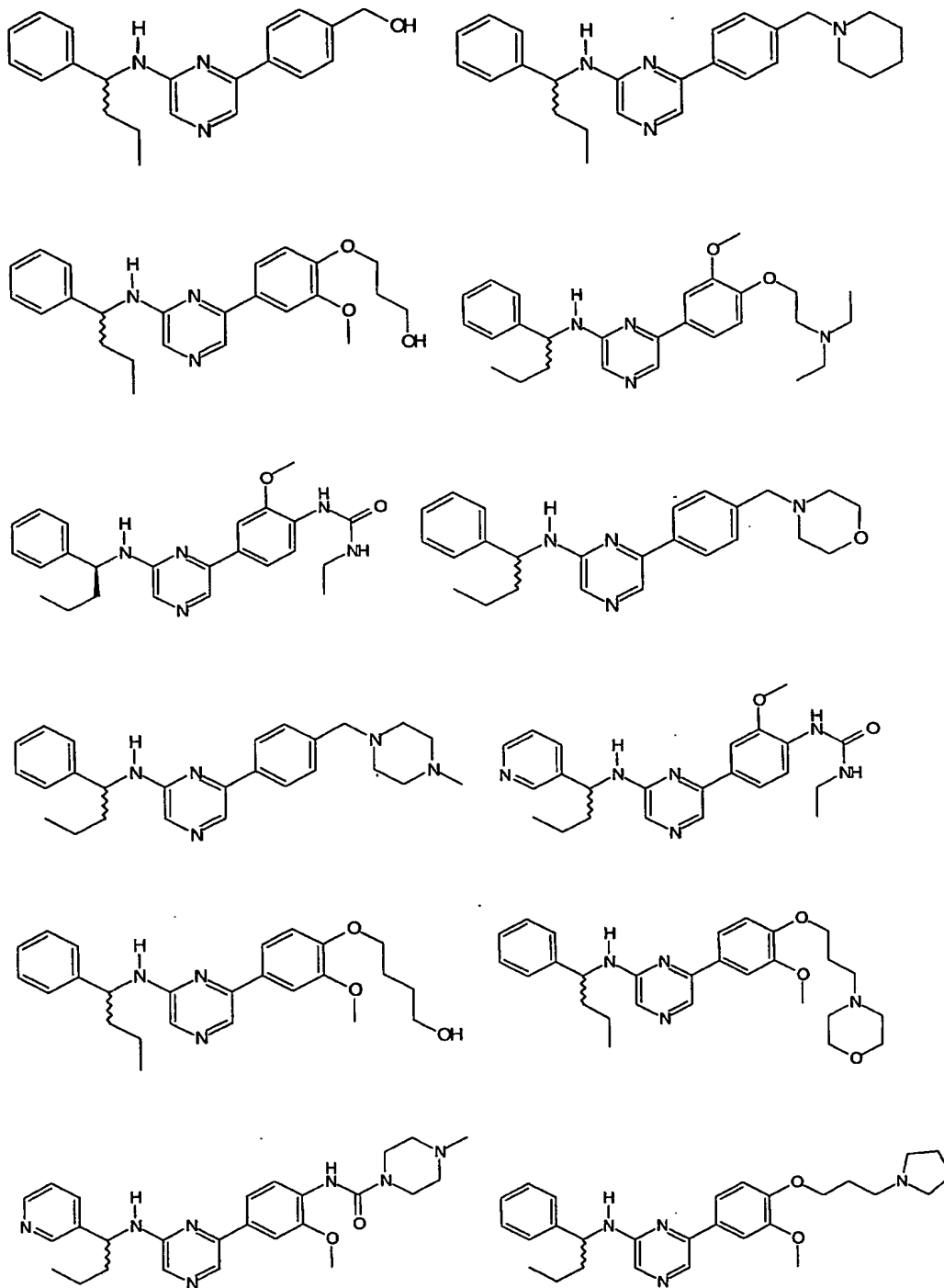
R₁₇ is selected from H, C₁₋₄ alkyl;

wherein when Y is CH₂R₁₂ then R₁₂ is not H, C₁₋₂alkyl.

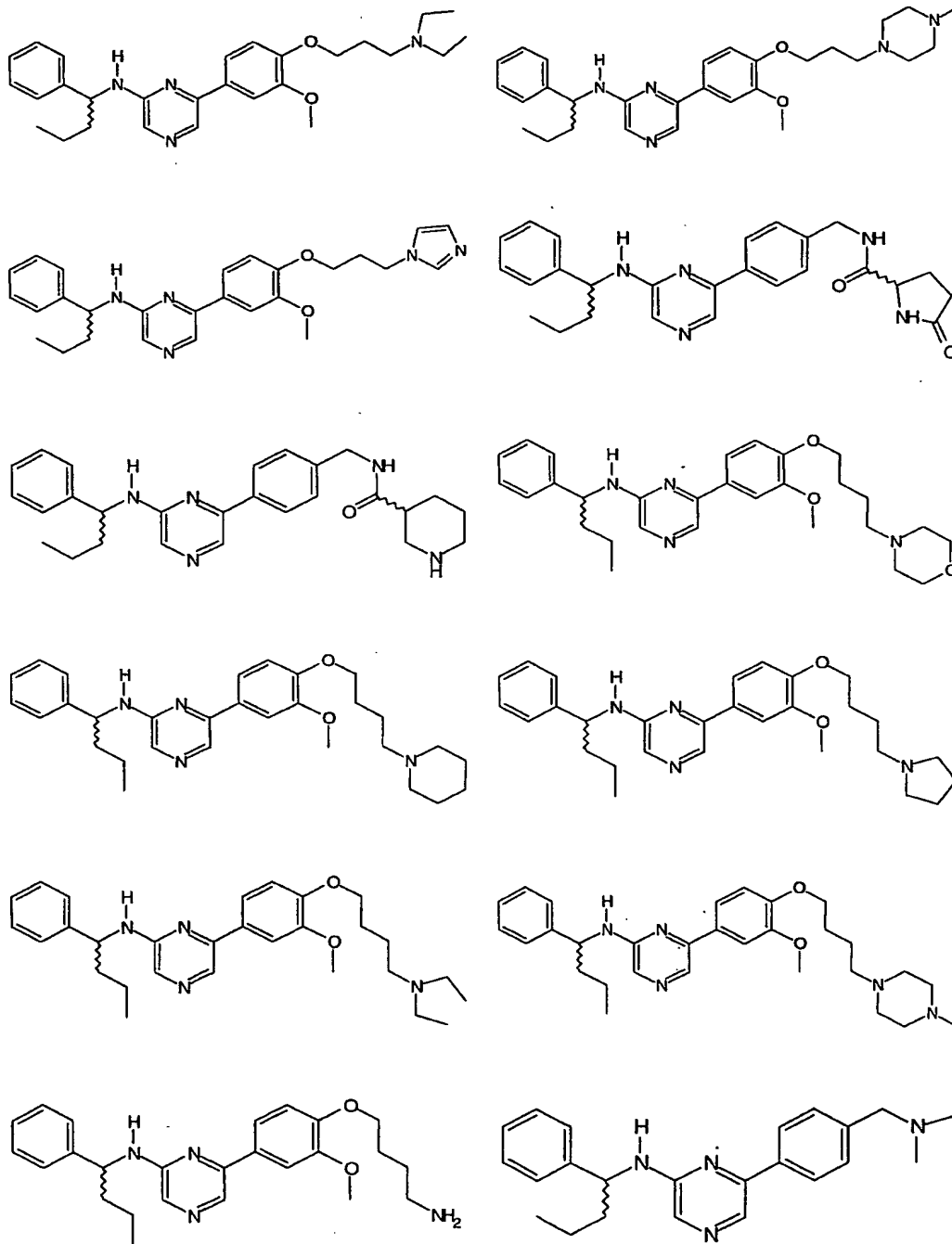
6. A compound according to claim 5 selected from the group consisting of:



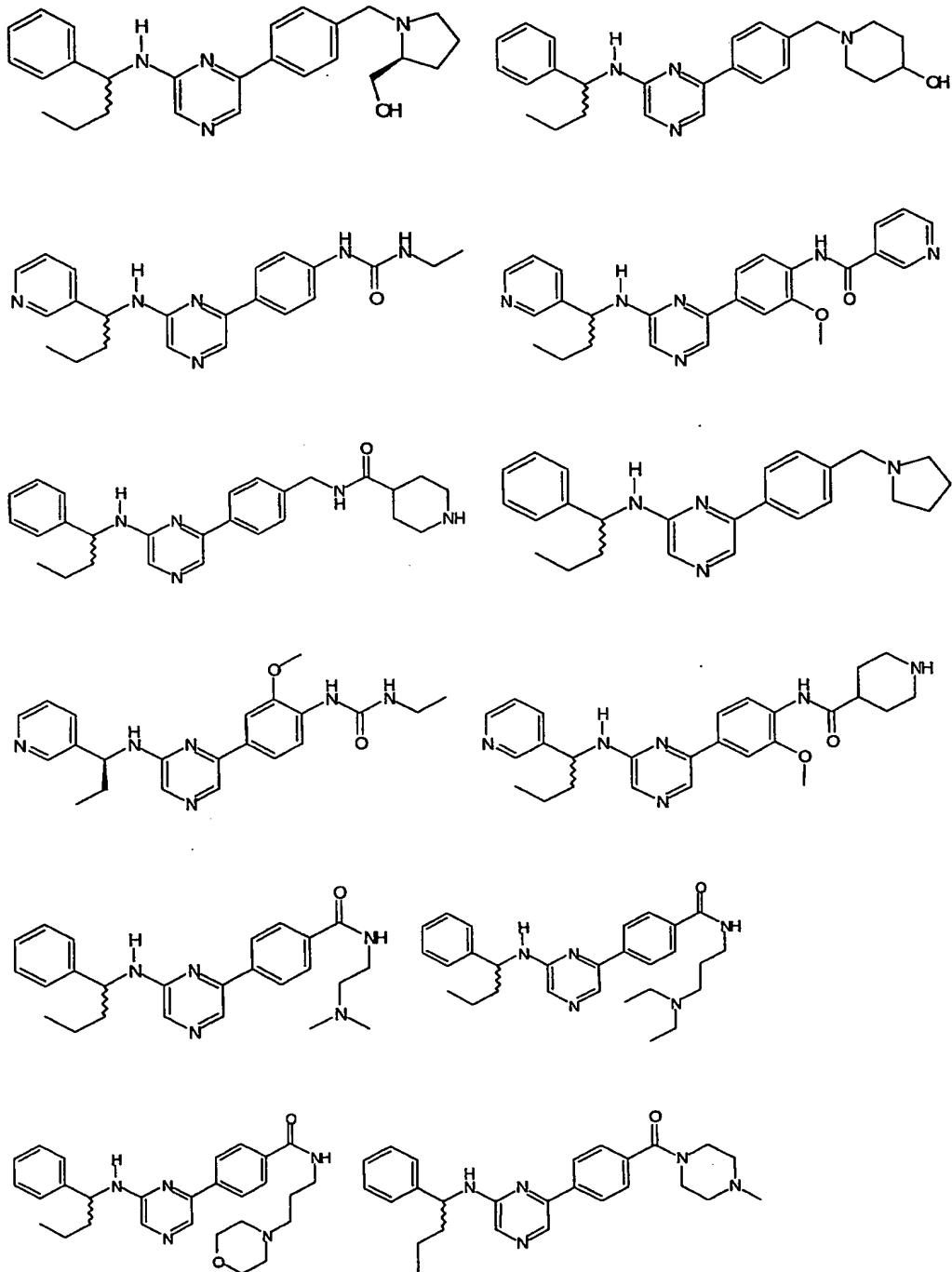
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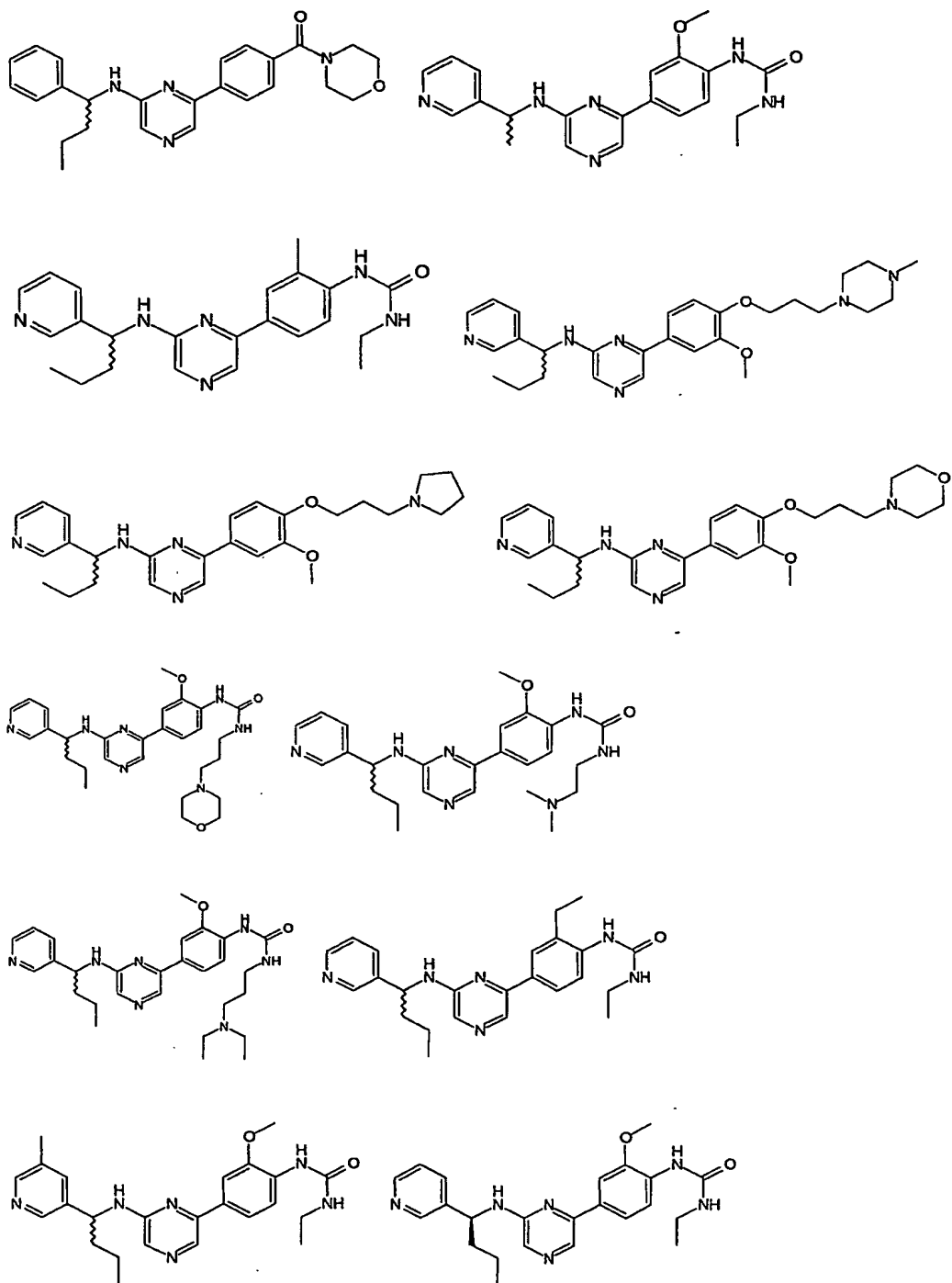
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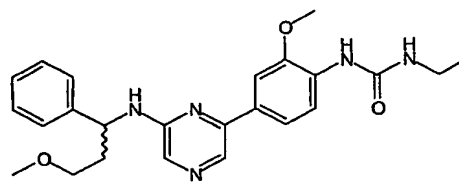
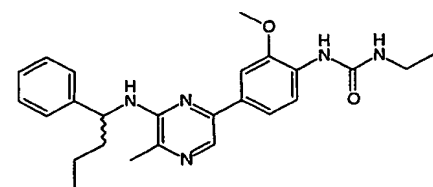
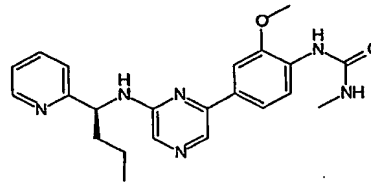
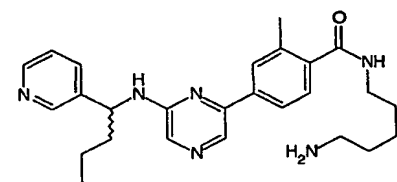
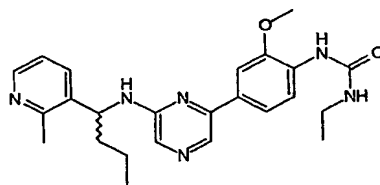
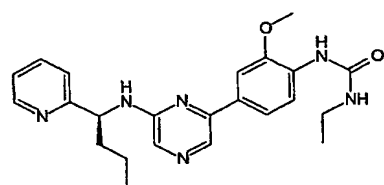
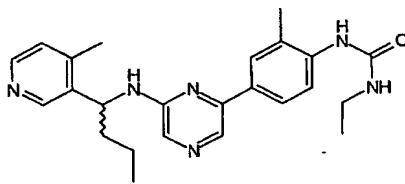
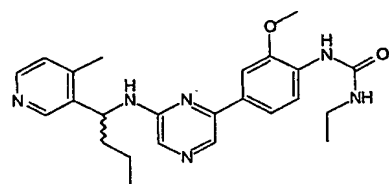
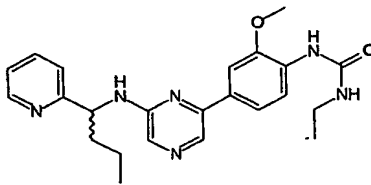
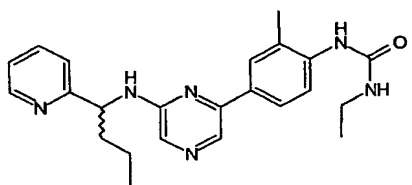
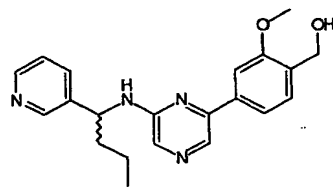
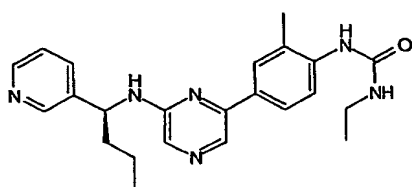
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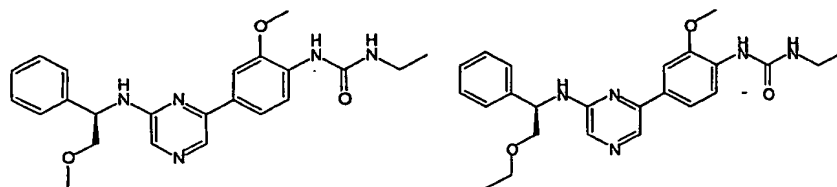
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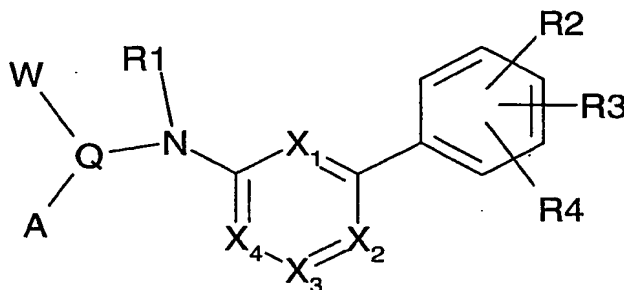
80.



81.



7. A compound of the general formula (III)



III

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

X_1, X_2, X_3, X_4 are selected from the following:

- (i) X_1 and X_2 are N and X_3 and X_4 are C independently substituted with Y;
- (ii) X_1 and X_4 are N and X_2 and X_3 are C independently substituted with Y;
- (iii) X_1 and X_3 are N and X_2 and X_4 are C independently substituted with Y;
- (iv) X_2 and X_4 are N and X_1 and X_3 are C independently substituted with Y;
- (v) X_1 is N and X_2, X_3 , and X_4 are C independently substituted with Y;

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- (vi) X_3 is N and X_1 , X_2 , and X_4 are C independently substituted with Y;
- (vii) X_4 is N and X_1 , X_2 , and X_3 are C independently substituted with Y;
- (viii) X_2 is N and X_1 , X_3 , and X_4 are C independently substituted with Y; and
- (ix) X_1 , X_2 and X_3 are N and X_4 is C substituted with Y;

R1 is H, C_{1-6} alkyl, C_{1-6} alkylNR5R6, C_{1-6} alkylNR5COR6, C_{1-6} alkylNR5SO₂R6, C_{1-6} alkylCO₂R5, C_{1-6} alkylCONR5R6, where R5 and R6 are each independently H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R7 is selected from H, C_{1-4} alkyl;

R2 is selected from C_{1-6} alkylOH, OC₂₋₆alkylOH, C_{1-6} alkylNR8R9, OC₂₋₆alkylNR8R9, C_{1-6} alkylNR8COR9, OC₂₋₆alkylNR8COR9, C_{1-6} alkylhetaryl, OC₂₋₆alkylhetaryl, OCONR8R9, NR8COOR9, NR10CONR8R9, CONR8R9, NR8COR12;

R8, R9 are each independently H, C_{1-4} alkyl, C_{1-4} alkylNR11R13, hetaryl, cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R12 is C_{2-4} alkyl, C_{1-4} alkylNR11R13, hetaryl, cyclohetalkyl;

R11, R13 are each independently H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R14 is selected from H, C_{1-4} alkyl;

R10 is H, C_{1-4} alkyl;

R3 and R4 are each independently H, halogen, C_{1-4} alkyl, OH, OC₁₋₄alkyl, CF₃, OCF₃;

Q is a bond, or C_{1-4} alkyl;

W is selected from H, C_{1-4} alkyl, C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC₁₋₄alkyl, NR15R16;

83.

R15, and R16 are each independently H, C₁₋₄alkyl, C₁₋₄alkyl cycloalkyl, C₁₋₄alkyl cyclohetalkyl, aryl, hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR17;

R17 is selected from H, C₁₋₄alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR18R19, Oaryl, Ohetaryl, CO₂R18, CONR18R19, NR18R19, C₁₋₄ alkylNR18R19, NR20C₁₋₄alkylNR18R19, NR18COR19, NR20CONR18R19, NR18SO₂R19;

R18, R19 are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cyclohetalkyl, aryl, hetaryl, C₁₋₄alkyl aryl, C₁₋₄ alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR21;

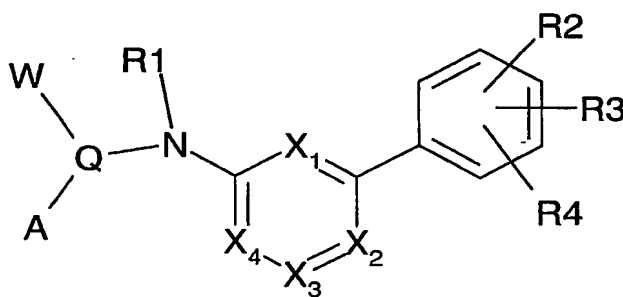
R21 is selected from H, C₁₋₄alkyl;

R20 is selected from H, C₁₋₄alkyl;

Y is selected from H, C₁₋₄alkyl, OH, NR22R23;

R22, R23 are each independently H, C₁₋₄alkyl.

8. A compound according to formula (III) of claim 7, wherein the compound is of the general formula (IV)



IV

or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

X₁, X₂, X₃, X₄ are selected from the following:

84.

- (i) X_1 and X_2 are N and X_3 and X_4 are C independently substituted with Y;
- (ii) X_1 and X_4 are N and X_2 and X_3 are C independently substituted with Y;
- (iii) X_1 and X_3 are N and X_2 and X_4 are C independently substituted with Y;
- (iv) X_2 and X_4 are N and X_1 and X_3 are C independently substituted with Y;
- (v) X_1 is N and X_2 , X_3 , and X_4 are C independently substituted with Y;
- (vi) X_3 is N and X_1 , X_2 , and X_4 are C independently substituted with Y;
- (vii) X_4 is N and X_1 , X_2 , and X_3 are C independently substituted with Y;
- (viii) X_2 is N and X_1 , X_3 , and X_4 are C independently substituted with Y; and
- (ix) X_1 , X_2 and X_3 are N and X_4 is C substituted with Y;

R_1 is H, C_{1-6} alkyl, C_{1-6} alkylNR₅R₆, where R_5 and R_6 are each independently H, C_{1-4} alkyl, aryl, hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₇;

R_7 is selected from H, C_{1-4} alkyl;

R_2 is selected from C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR₈R₉, OC_{2-6} alkylNR₈R₉, C_{1-6} alkylNR₈COR₉, OC_{2-6} alkylNR₈COR₉, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, $OCONR_8R_9$, NR_8COOR_9 , $NR_{10}CONR_8R_9$, $CONR_8R_9$, NR_8COR_{12} ;

R_8 , R_9 are each independently H, C_{1-4} alkyl, C_{1-4} alkylNR₁₁R₁₃, hetaryl, cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₁₄;

R_{12} is C_{2-4} alkyl, C_{1-4} alkylNR₁₁R₁₃, hetaryl, cyclohetalkyl;

R_{11} , R_{13} are each independently H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₁₄;

R_{14} is selected from H, C_{1-4} alkyl;

R_{10} is H, C_{1-4} alkyl;

85.

R3 and R4 are each independently H, halogen, C₁₋₄alkyl, OH, OC₁₋₄alkyl, CF₃, OCF₃;

Q is CH;

W is selected from C₁₋₄alkyl, C₂₋₆alkenyl; where C₁₋₄alkyl or C₂₋₆alkenyl may be optionally substituted with C₁₋₄alkyl, OH, OC₁₋₄alkyl, NR₁₅R₁₆;

R₁₅, and R₁₆ are each independently H, C₁₋₄alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₁₇;

R₁₇ is selected from H, C₁₋₄alkyl;

A is aryl, hetaryl optionally substituted with 0-2 substituents independently chosen from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR₁₈R₁₉, Oaryl, Ohetaryl, CO₂R₁₈, CONR₁₈R₁₉, NR₁₈R₁₉, C₁₋₄ alkylNR₁₈R₁₉, NR₂₀C₁₋₄alkylNR₁₈R₁₉, NR₁₈COR₁₉, NR₂₀CONR₁₈R₁₉, NR₁₈SO₂R₁₉;

R₁₈, R₁₉ are each independently H, C₁₋₄alkyl, C₁₋₄alkyl cyclohetalkyl, aryl, hetaryl, C₁₋₄alkyl aryl, C₁₋₄alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₂₁;

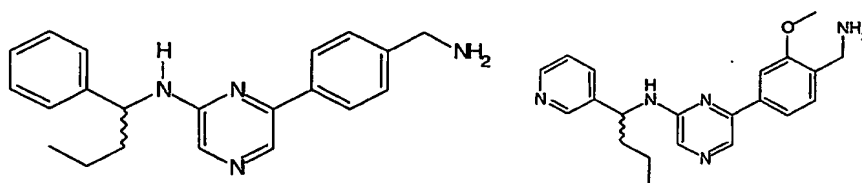
R₂₁ is selected from H, C₁₋₄alkyl;

R₂₀ is selected from H, C₁₋₄alkyl;

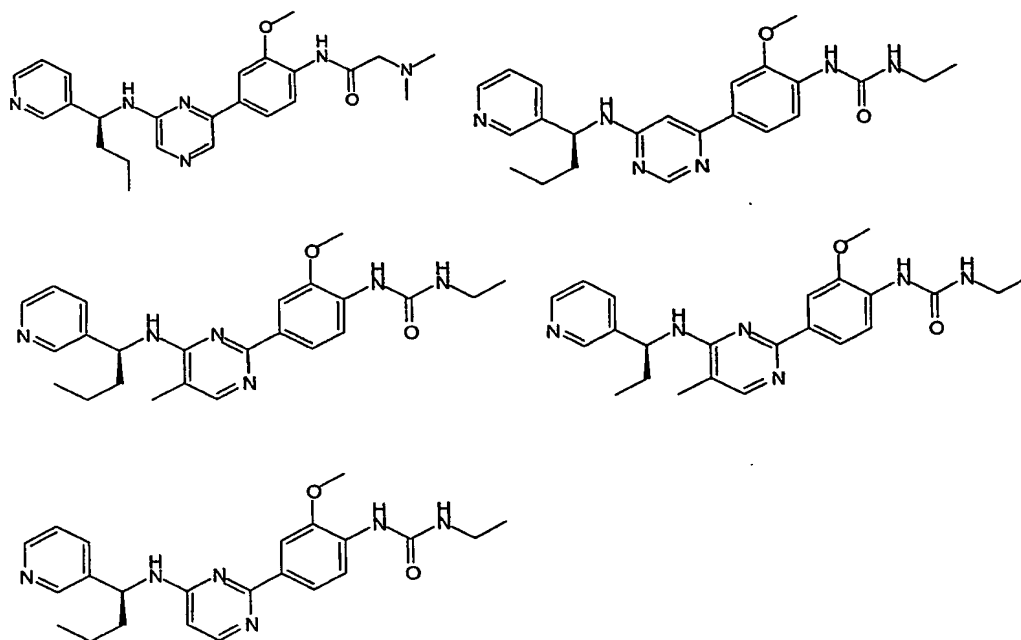
Y is selected from H, C₁₋₄alkyl, NR₂₂R₂₃;

R₂₂, R₂₃ are each independently H, C₁₋₄alkyl.

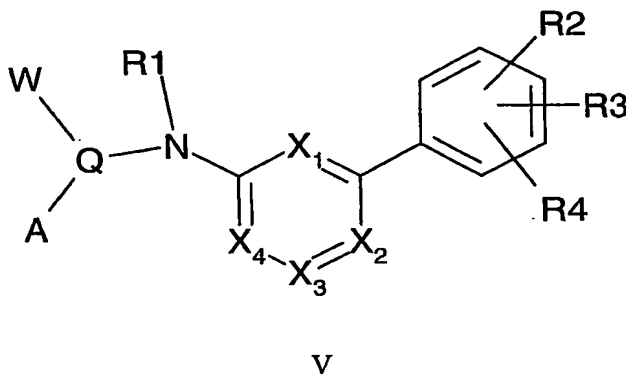
9. A compound according to claim 7 wherein the compound is selected from the group consisting of:



86.



10. A compound of the general formula (V)



or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

X₁, X₂, X₃, X₄ are selected from the following:

(i) X₁ and X₂ are N and X₃ and X₄ are C independently substituted with Y;

87.

- (ii) X_1 and X_4 are N and X_2 and X_3 are C independently substituted with Y;
- (iii) X_2 and X_4 are N and X_1 and X_3 are C independently substituted with Y;
- (iv) X_1 is N and X_2 , X_3 , and X_4 are C independently substituted with Y;
- (v) X_3 is N and X_1 , X_2 , and X_4 are C independently substituted with Y;
- (vi) X_4 is N and X_1 , X_2 , and X_3 are C independently substituted with Y;
- (vii) X_2 is N and X_1 , X_3 , and X_4 are C independently substituted with Y; and
- (viii) X_1 , X_2 and X_3 are N and X_4 is C substituted with Y;

R1 is H, C_{1-6} alkyl, C_{1-6} alkylNR5R6, C_{1-6} alkylNR5COR6, C_{1-6} alkylNR5SO₂R6, C_{1-6} alkylCO₂R5, C_{1-6} alkylCONR5R6, where R5 and R6 are each independently H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, C_{1-4} alkylhetaryl or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR7;

R7 is selected from H, C_{1-4} alkyl;

R2 is selected from OH, OC $_{1-6}$ alkyl, C_{1-6} alkylOH, OC $_{2-6}$ alkylOH, C_{1-6} alkylNR8R9, OC $_{2-6}$ alkylNR8R9, C_{1-6} alkylNR8COR9, OC $_{2-6}$ alkylNR8COR9, C_{1-6} alkylhetaryl, OC $_{2-6}$ alkylhetaryl, OCONR8R9, NR8COOR9, NR10CONR8R9, CONR8R9, NR8COR12;

R8, R9 are each independently H, C_{1-4} alkyl, C_{1-4} alkylNR11R13, hetaryl, cyclohetalkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R12 is C_{2-4} alkyl, C_{1-4} alkylNR11R13, hetaryl, cyclohetalkyl;

R11, R13 are each independently H, C_{1-4} alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14;

R14 is selected from H, C_{1-4} alkyl;

R10 is H, C_{1-4} alkyl;

R3 and R4 are each independently H, halogen, C_{1-4} alkyl, OH, OC $_{1-4}$ alkyl, CF₃, OCF₃;

88.

Q is a bond, or C₁₋₄alkyl;

W is selected from H, C₁₋₄alkyl, C₂₋₆alkenyl; where C₁₋₄alkyl or C₂₋₆alkenyl may be optionally substituted with C₁₋₄alkyl, OH, OC₁₋₄alkyl, NR₁₅R₁₆;

R₁₅, and R₁₆ are each independently H, C₁₋₄alkyl, C₁₋₄alkyl cycloalkyl, C₁₋₄alkyl cyclohetalkyl, aryl, hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₁₇;

R₁₇ is selected from H, C₁₋₄alkyl;

A is aryl, hetaryl optionally substituted with 0-3 substituents independently chosen from halogen, C₁₋₄ alkyl, CF₃, aryl, hetaryl, OCF₃, OC₁₋₄alkyl, OC₂₋₅alkylNR₁₈R₁₉, Oaryl, Ohetaryl, CO₂R₁₈, CONR₁₈R₁₉, NR₁₈R₁₉, C₁₋₄ alkylNR₁₈R₁₉, NR₂₀C₁₋₄alkylNR₁₈R₁₉, NR₁₈COR₁₉, NR₂₀CONR₁₈R₁₉, NR₁₈SO₂R₁₉;

R₁₈, R₁₉ are each independently H, C₁₋₄ alkyl, C₁₋₄ alkyl cyclohetalkyl, aryl, hetaryl, C₁₋₄alkyl aryl, C₁₋₄ alkyl hetaryl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR₂₁;

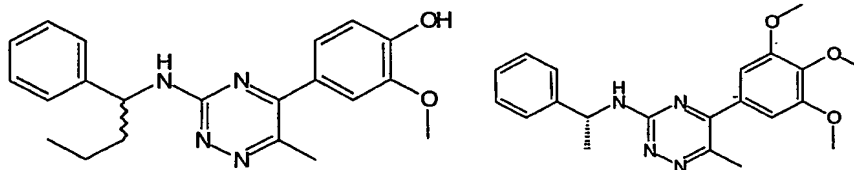
R₂₁ is selected from H, C₁₋₄ alkyl;

R₂₀ is selected from H, C₁₋₄ alkyl;

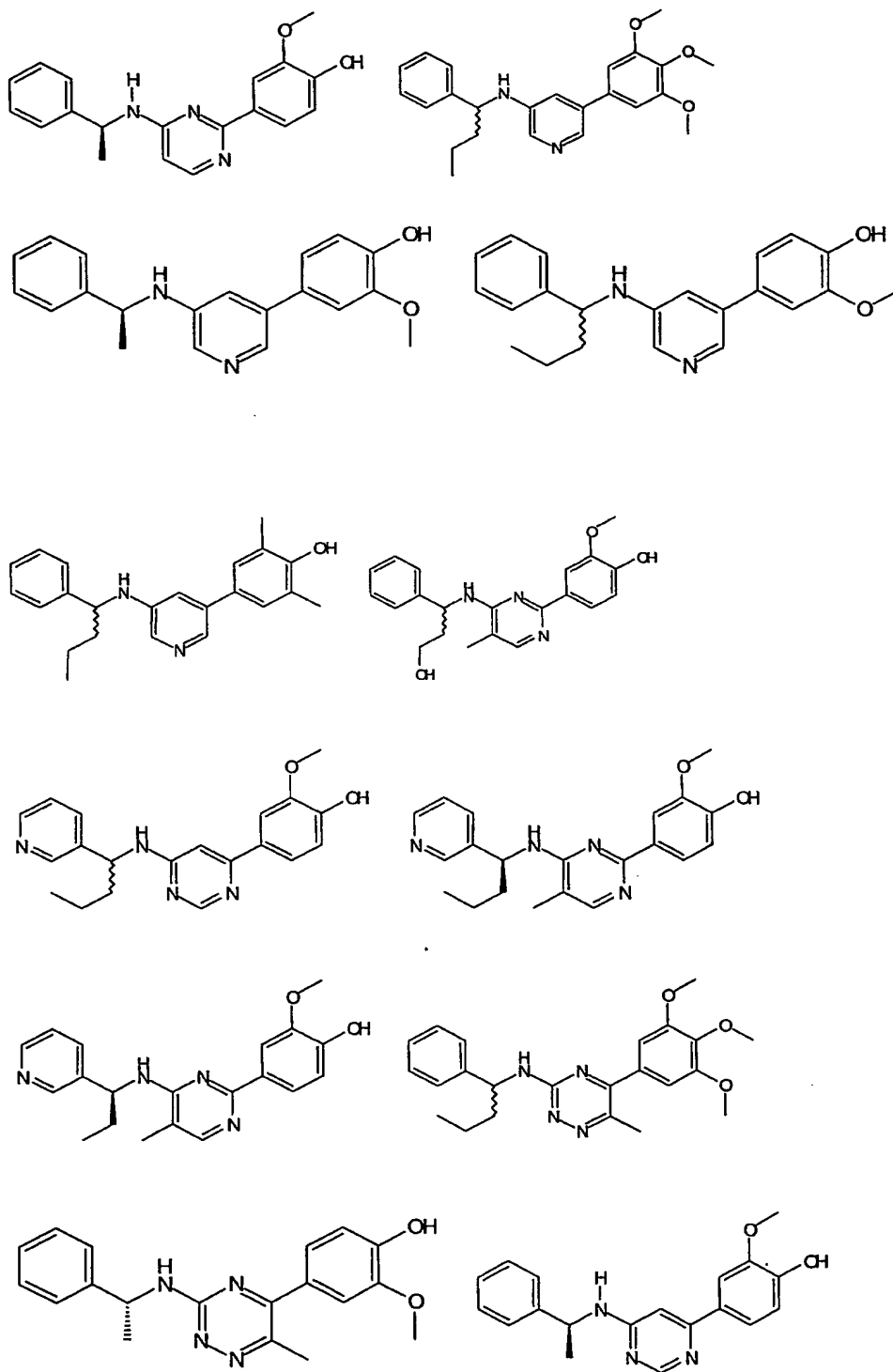
Y is selected from H, C₁₋₄alkyl, OH, NR₂₂R₂₃;

R₂₂, R₂₃ are each independently H, C₁₋₄ alkyl.

11. A compound according to claim 10 selected from the group consisting of:

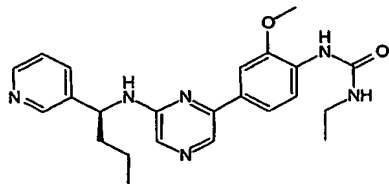


89.



90.

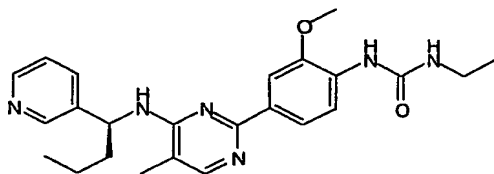
12. A compound of the formula:



or a pharmaceutically acceptable prodrug, salt, hydrate, solvate, crystal form or a diastereomer thereof

91.

13. A compound of the formula:



or a pharmaceutically acceptable prodrug, salt, hydrate, solvate, crystal form or a diastereomer thereof

14. A composition comprising a carrier and at least one compound according to any one of claims 5 to 13.
15. A method of treatment of a hyperproliferation-related disorder or disease state in a subject, said method comprising administering a therapeutically effective amount of at least one compound according to any one claims 1 to 13 or a composition according to 14.
16. A method of treatment according to claim 15, wherein the hyperproliferation-related disorder or disease state is treatable by the modulation of microtubule polymerisation.
17. A method according to claim 15 or claim 16, wherein the hyperproliferation-related disorder or disease state is selected from the group consisting of Cancer, infectious diseases, vascular restenosis or inflammatory diseases.
18. A method of treatment of a protein-kinase related disorder or disease state in a subject, said method comprising administering a therapeutically effective amount of at least one compound according to any one of claims 1 to 13 or a composition according to 14.
17. A method according to claim 18, wherein the protein-kinase related disorder or disease state is selected from the group consisting of Atopy, Cell Mediated Hypersensitivity, Rheumatic Diseases, Other autoimmune diseases and Viral Diseases.
18. A method of treatment of diseases and conditions associated with inflammation and infection in a subject, said method comprising administering a therapeutically effective amount of at least one compound according to any one of claims 1 to 13 or a composition according to claim 14.